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EXAMINER	
NICHOLS, CHRISTOPHER J	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/830,972	SCHWAB ET AL.	
	Examin r	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication app ars on the cov r she t with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21,50,51 and 54* is/are pending in the application.

4a) Of the above claim(s) *22-49,52,53 and 55-97* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-21, 50, 51, and 54* is/are rejected.

7)☒ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-97* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *24 September 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group 1 (claims 1-21, 50, 51, and 54 (each in part)) in the Response filed 1 December 2003 is acknowledged. The traversal is on the ground(s) that there is a technical relationship among the different groups that involves at least one common special technical feature, Spillmann *et al.* (1998) does not teach a purified Nogo protein free of myelin material with which Nogo is natively associated, and all three Nogo proteins A, B, and C share in common the sequence of Exon 3. This is not found persuasive because Lack of Unity was found on the grounds that unity of invention exists only when the shared some or corresponding technical feature is a contribution over the prior art (PCT Rule 13.2). The inventions listed as Groups 1-31 in the previous Office Action (28 August 2003) does not related to a single general inventive concept because they lack the same or corresponding special technical feature. The special technical feature of Group 1 is a purified Nogo protein which is taught by Spillmann *et al.* (1998) who does in fact teach a "Nogo protein that is free of all central nervous system myelin material with which it is natively associated" as per pp. 19284 wherein Spillmann *et al.* (1998) clearly shows SDS-polyacrylamide gel bands of purified bNI-220 in the absence of any myelin (Figure 12). Therefore regardless of alleged shared technical features, the special technical feature of Group 1 is not a contribution over the prior art and thus no unity of invention is present for Groups 1-34. Claims **22-49, 52, 53,** and **55-97** are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. The requirement is still deemed proper and is therefore made FINAL.

2. However, as a courtesy to the Applicant, claims 1-21, 50, 51, and 54 will be examined to the extent that they read on SEQ ID NO: 2, 28, 29, and 32.

Drawings

3. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference sign(s) not mentioned in the description: Figure 2 contains "2A1-2A4", Figure 12 contains "12A-12D", Figure 14 contains "14A-14C". A proposed drawing correction, corrected drawings, or amendment to the specification to add the reference sign(s) in the description, are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (pp. 16 lines 6, 27, & 33). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims **1-13, 16-18, 20,** and **21** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *a purified Nogo protein comprising or consisting of SEQ ID NO: 2, SEQ ID NO: 29, SEQ ID NO: 32 wherein said proteins are glycosylated or unglycosylated* does not reasonably provide enablement for *any other as of yet unspecified, unknown, and/or uncharacterized Nogo proteins, as of yet undisclosed chimeric proteins, proteins encoded by nucleic acids which hybridize to SEQ ID NO: 1 and/or SEQ ID NO: 28, or fragments thereof.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to **make** or **use** the invention commensurate in scope with these claims.

6. The claims are drawn very broadly to any and all Nogo proteins. The language of said claims encompasses all isoforms of Nogo in known mammalian species.

7. The specification teaches that SEQ ID NO: 2 encodes rat Nogo A, SEQ ID NO: 30 encodes human Nogo, SEQ ID NO: 31 encodes SEQ ID NO: 32, rat Nogo C. The Specification is silent on the structure and/or sequence of Nogo B. It is suggested in the Specification that Nogo A, B, and C may arise from alternative splicing and/or transcription.

8. The specification fails to provide any guidance for the successful isolation and characterization of such a breadth of proteins, and since resolution of the various complications in regards to isolating and characterizing a protein is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* isolation and characterization of an unknown number of potential

Nogo candidates to correlate with the known examples. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

9. Additionally, a person skilled in the art would recognize that predicting the efficacy of undertaking such an endeavor based solely on a few examples as highly problematic (see MPEP §2164.01). Thus, although the specification prophetically considers and discloses general methodologies of isolating and characterizing all known and unknown Nogo proteins, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

10. The following references are cited herein to illustrate the state of the art of protein biochemistry.

11. Regarding sequence derivatives of Nogo proteins, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of

success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et al.* (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein

structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39, especially p. 36 at Box 2; Doerks *et al.*, (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427]. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

12. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from prophetic consideration and guidance to actual isolation and characterization of all Nogo proteins, derivatives, fragments, and homologues as exemplified in the references herein.

13. Claims **14, 15, 19, 50, 51,** and **54** are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which

was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

14. The claims are drawn very broadly to any and all Nogo proteins as well as a number of fragments, derivatives, and variants. The language of said claims encompasses all isoforms of Nogo in known mammalian species.

15. The specification teaches that SEQ ID NO: 2 encodes rat Nogo A, SEQ ID NO: 30 encodes human Nogo, SEQ ID NO: 31 encodes SEQ ID NO: 32, rat Nogo C. The Specification is silent on the structure and/or sequence of Nogo B. It is suggested in the Specification that Nogo A, B, and C may arise from alternative splicing and/or transcription.

16. The specification fails to provide any guidance for the successful isolation and characterization of such a breadth of proteins, and since resolution of the various complications in regards to isolating and characterizing a protein is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the art as outlined below, the quantity of experimentation required to practice the invention as claimed would require the *de novo* isolation and characterization of an unknown number of potential Nogo candidates to correlate with the known examples. In the absence of any guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

17. Additionally, a person skilled in the art would recognize that predicting the efficacy of undertaking such an endeavor based solely on a few examples as highly problematic (see MPEP §2164.01). Thus, although the specification prophetically considers and discloses general

methodologies of isolating and characterizing all known and unknown Nogo proteins, such a disclosure would not be considered enabling since the state of protein biochemistry is highly unpredictable. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

18. The following references are cited herein to illustrate the state of the art of protein biochemistry.

19. Regarding sequence derivatives of Nogo proteins, the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions [see Wells (18 September 1990) "Additivity of Mutational Effects in Proteins." Biochemistry **29**(37): 8509-8517; Ngo *et*

al. (2 March 1995) "The Protein Folding Problem and Tertiary Structure Prediction, Chapter 14: Computational Complexity Protein Structure Prediction, and the Levinthal Paradox" pp. 492-495]. However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. The art recognizes that function cannot be predicted from structure alone [Bork (2000) "Powers and Pitfalls in Sequence Analysis: The 70% Hurdle." Genome Research **10**:398-400; Skolnick and Fetrow (2000) "From gene to protein structure and function: novel applications of computational approaches in the genomic era." Trends in Biotech. **18**(1): 34-39, especially p. 36 at Box 2; Doerks *et al.*, (June 1998) "Protein annotation: detective work for function prediction." Trends in Genetics **14**(6): 248-250; Smith and Zhang (November 1997) "The challenges of genome sequence annotation or 'The devil is in the details'." Nature Biotechnology **15**:1222-1223; Brenner (April 1999) "Errors in genome annotation." Trends in Genetics **15**(4): 132-133; Bork and Bairoch (October 1996) "Go hunting

in sequence databases but watch out for the traps." Trends in Genetics **12**(10): 425-427]. Due to the large quantity of experimentation necessary to generate the infinite number of derivatives recited in the claims and possibly screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

20. Thus the specification of the instant application fails to provide adequate guidance for one of skill in the art to overcome the unpredictability and challenges of applying results from prophetic consideration and guidance to actual isolation and characterization of all Nogo proteins, derivatives, fragments, and homologues as exemplified in the references herein.

21. Claims **1, 2, 5, 8-19, 20, 21, 50, 51,** and **54** are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

22. Claim 1 requires only that the protein be "A Nogo protein that is free of all central nervous system myelin material with which it is natively associated" thus implying that the Nogo protein's identity is not known or must be confirmed. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a

specific biological activity. Thus, the claims are drawn to protein that is defined by the absence of CNS material.

23. Claim 2 requires that the protein be "Nogo A" or "Nogo B" while the Specification only provides examples of rat Nogo A and no examples of Nogo B. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to protein that is defined by membership in a genus.

24. Claim 5 requires that the protein be "Nogo C" while the Specification only provides a single example of rat Nogo C. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to protein that is defined by membership in a genus.

25. Claim 17 requires that the protein be "Nogo A. Nogo B, or Nogo C" while the Specification only provides examples consisting of rat Nogo A and rat Nogo C. The Specification is silent on examples of Nogo B. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to protein that is defined by membership in a genus.

26. Claim 19 requires only that the protein be "chimeric protein" comprising fragment of a protein fused by a covalent bound to a least a portion of a second protein which is different from said fragment thus implying that the chimeric protein's identity is not known or must be confirmed. The claims do not require that the polypeptide possess any particular conserved

structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to protein that is defined by being a chimera or fusion of two different proteins.

27. Claims 20 and 21 requires only that the product be a "purified molecule" comprising fragment thus implying that the molecule's identity is not known or must be confirmed. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. The art recognizes that "molecule" can pertain to chemical entities, pharmaceutical compositions, proteins, peptides, non-peptide compounds, animal tissue extracts, vegetable extracts, cell extracts, synthetic agents, biologically derived substances as well as proteinaceous substances, known, and unknown compounds. Thus, the claims are drawn to protein that is defined by being a purified molecule of unknown structure.

28. The Specification only provides the sequence for rat Nogo C (SEQ ID NO: 31 & 32), not other species.

29. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of a broad genus ("Nogo", "chimeras", "molecules"). The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not

described. Accordingly, the specification does not provide adequate written description of the claimed genus.

30. To satisfy the written-description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing. *Vas-Cath*, 935 F.3d at 1563; see also *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572 [41 USPQ2d 1961] (Fed. Cir. 1997) (patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention"); *In re Gosteli*, 872 F.2d 1008, 1012 [10 USPQ2d 1614] (Fed. Cir. 1989) ("the description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed"). Thus, an applicant complies with the written-description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572.

31. See *University of Rochester v. G.D. Searle & Co.*, 68 USPQ2d 1424 (DC WNY 2003). In *University of Rochester v. G.D. Searle & Co.* a patent directed to method for inhibiting prostaglandin synthesis in human host using unspecified compound, in order to relieve pain without side effect of stomach irritation, did not satisfy written description requirement of 35 U.S.C. §112, since patent described the compound's desired function of reducing activity of enzyme PGHS-2 without adversely affecting PGHS-1 enzyme activity, but did not identify said compound, since invention consists of performing "assays" to screen compounds in order to discover those with desired effect, but patent did not name even one compound that assays would

identify as suitable for practice of invention, or provide information such that one skilled in art could identify suitable compound, since specification did not indicate that compounds are available in public depository, since claimed treatment method cannot be practiced without compound, and since inventors thus cannot be said to have "possessed" claimed invention without knowing of compound or method certain to produce compound. Thus said patent constituted an invitation to experiment to first identify, then characterize, and then use a therapeutic a class of compound defined only by their desired properties.

32. Therefore the full breadth of the claim fails to meet the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

33. Claim **12** is are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

34. The claims are drawn to polypeptides having at least 50% sequence identity with a particular disclosed sequence. The claims do not require that the polypeptide possess any particular conserved structure, or other distinguishing feature, such as a specific biological activity. Thus, the claims are drawn to a genus of polypeptides that is defined by sequence identity.

35. To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus.

The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, and any combination thereof. In this case, the only factor present in the claim that is sufficiently disclosed is a partial structure in the form of a recitation of percent identity. The specification does not identify any particular portion of the structure that must be conserved, nor does it provide a disclosure of structure/function correlation. The distinguishing characteristics of the claimed genus are not described. The only adequately described species is a polypeptide comprising **SEQ ID NO: 2**. No active variants are disclosed. Accordingly, the specification does not provide adequate written description of the claimed genus.

36. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

37. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

38. Therefore, only isolated polypeptides comprising the amino acid sequence set forth in **SEQ ID NO: 2**, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision.

39. Claims **13** and **18** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "hybridizable" in claim 13 is a relative term which renders the claim indefinite. The term " hybridizable" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Neither the specification nor the art defines the term unambiguously. Thus the metes and bounds of the claims cannot be determined.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for

> patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

40. Claims **1, 14,** and **20** are rejected under 35 U.S.C. 102(a) as being anticipated by Spillmann *et al.* (24 July 1998) "Identification and Characterization of a Bovine Neurite Growth Inhibitor (bNI-220)." The Journal of Biological Chemistry **273**(30): 19283-19293.

41. Spillmann *et al.* (1998) teaches a "Nogo protein that is free of all central nervous system myelin material with which it is natively associated" as per pp. 19284 wherein Spillmann *et al.* (1998) clearly shows SDS-polyacrylamide gel bands of purified bNI-220 in the absence of any myelin thus meeting the limitations of claim 1 (Figure 12). While silent on whether or not bNI-220 (a Nogo protein) is able to be bound by an antibody directed against a Nogo protein, a compound and all of its properties are inseparable [*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963))]. Therefore since bNI-220 is a purified protein free of all central nervous system myelin material it is inherent that said protein could be bound by an antibody specific for an epitope thereof the meeting the limitations of claims 14 and 20.

42. Claims **1, 2, 3, 9, 10, 12, 13, 14, 15, 16, 18, 19, 20,** and **21** are rejected under 35 U.S.C. 102(e) as being anticipated by US 2002/0072493 (13 June 2002) Eisenbach-Schwartz *et al.*

43. The instant claims require a Nogo protein be free of all CNS myelin material, be it Nogo or SEQ ID NO: 2 of the instant Application.

44. US 2002/0072493 teaches Nogo proteins including rat Nogo and human Nogo, the Examiner notes that the Nogo proteins of US 2002/0072493 may be "isolated or purified"

([**0096-0100**]) thus meeting the limitations of claims 1, 2, 5, 9, 10 ([**0024, 0122**]). SEQ ID NO: 17 of US 2002/0072493 is also taught to be rat species Nogo A thus meeting the limitations of claim 2 (Example 5). US 2002/0072493 also teaches a sequence that shares 100% homology to SEQ ID NO: 2 thus meeting the limitations of claims 3 and 16 (SEQ ID NO: 17 therein pp. 44-47).

45. Concerning claims 12, 13, and 18, US 2002/0072493 teaches that the "NS-specific antigens" nucleic acids which hybridize to the sequences therein including also include amino acid sequences that are 60% or greater as determined by computer programs including but not limited to BLASTP.

46. While US 2002/0072493 is silent on whether or not the Nogo proteins (rat Nogo and human Nogo) are able to be bound by an antibody directed against a Nogo protein, a compound and all of its properties are inseparable [*In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963))]. Therefore since the Nogo proteins disclosed therein are purified free of all central nervous system myelin material it is inherent that said protein could be bound by an antibody specific for an epitope thereof the meeting the limitations of claims 14-15 and 19-21.

Summary

47. No claims are allowed.

48. The following articles, patents, and published patent applications were found by the Examiner during the art search while not relied upon are considered pertinent to the instant application:

a. Morris *et al.* (1999) "Cloning and Characterization of a 22 kDa protein from rat adipocytes: a new member of the reticulon family." Biochim. Biophys. Acta **1450**: 68-76 (teaches a sequence with 100% homology to SEQ ID NO: 2)

b. Chen *et al.* (27 January 2000) "Nogo-A is a myelin-associated neurite outgrowth inhibitor and an antigen for monoclonal antibody IN-1." Nature **403**: 434-439 (teaches a sequence with 100% homology to SEQ ID NO: 2)

c. GrandPre *et al.* (30 May 2002) "Nogo-66 receptor antagonist peptide promotes axonal regeneration." Nature **417**(6888): 547-551 (teaches a sequence with 100% homology to SEQ ID NO: 2)

d. US 2002/0072493 (13 June 2002) Eisenbach-Schwartz *et al.* (teaches sequences with 72.3% homology to SEQ ID NO: 32, and 99.9% homology to residues 38-141 SEQ ID NO: 32)

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is **(571) 272-0889**. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on **(571) 272-0887**. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
February 5, 2004

ELIZABETH KEMMERER
PRIMARY EXAMINER